What is claimed is:

1. A method for identifying a candidate compound as a suitable pro-drug, comprising:

(a) providing the candidate compound having an esterified phosphonate group or an esterified carboxyl group;

(b) contacting the candidate compound with an extract capable of catalyzing the hydrolysis of a carboxylic ester to produce a metabolite compound; and

(c) identifying the candidate compound as a suitable pro-drug if the metabolite compound has a phosphonic acid group instead of the esterified phosphonate group of the candidate compound, or a carboxylic acid group instead of the esterified carboxyl group of the candidate compound.

2. The method of claim 1, wherein said extract is obtained from peripheral blood mononuclear cells.

3. A method for identifying a candidate compound as a suitable pro-drug, comprising:

(a) providing the candidate compound having an esterified phosphonate group or an esterified carboxyl group;

(b) contacting the candidate compound with an extract of peripheral blood mononuclear cells having carboxylic ester hydrolase activity to produce a metabolite compound; and

(c) identifying the candidate compound as a suitable pro-drug if the metabolite compound has a phosphonic acid group instead of the esterified phosphonate group of the candidate compound, or a carboxylic acid group instead of the esterified carboxyl group of the candidate compound.

4. The method of claim 3, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound known to have anti-HIV therapeutic activity with an esterified phosphonate or carboxyl group.

5. The method of claim 4, wherein said prototype compound is not a nucleoside, and does not contain a nucleoside base.

6. The method of claim 3, wherein said providing step comprises providing a candidate compound that is an amino acid phosphonoamidate, wherein a carboxyl group of the amino acid is esterified.

7. The method of claim 3, wherein said providing step comprises providing a candidate compound that is substantially stable against extracellular hydrolysis of the esterified group.

8. The method of claim 3, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound.

9. The method of claim 3, further comprising (d) determining the intracellular persistence of the candidate compound.

10. The method of claim 3, further comprising (d) determining the intracellular persistence of the metabolite compound.

11. The method of claim 3, further comprising (d) determining the intracellular persistence of the candidate compound and the metabolite compound.

12. The method of claim 3, further comprising (d) determining the tissue selectivity of the candidate compound.

13. The method of claim 3, further comprising (d) determining the tissue selectivity of the metabolite compound.

14. The method of claim 3, further comprising (d) determining the tissue selectivity of the candidate compound and the metabolite compound.

15. The method of claim 3, further comprising (d) determining the anti-HIV protease activity of the metabolite compound.

16. The method of claim 3, further comprising (d) determining the HIV-inhibition ability of the candidate compound.

17. The method of claim 3, further comprising (d) determining the resistance of HIV to the candidate compound.

18. The method of claim 3, further comprising (d) determining the resistance of HIV to the metabolite compound.

19. The method of claim 3, further comprising (d) determining the resistance of HIV to the candidate compound and the metabolite compound.

20. The method of claim 3, further comprising (d) determining the intracellular residence time of the candidate compound.

21. The method of claim 3, further comprising (d) determining the intracellular residence time of the metabolite compound.

22. The method of claim 3, further comprising (d) determining the intracellular residence time of the candidate compound and the metabolite compound.

23. The method of claim 20, wherein said step of determining the intracellular residence time of the candidate compound comprises determining the half-life of the candidate compound within lymphoid tissue.

24. The method of claim 21, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

25. The method of claim 22, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

26. The method of claim 23, wherein said step of determining the half-life of the candidate compound further comprises determining the half-life of the candidate compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

27. The method of claim 24, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

28. The method of claim 25, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

29. The method of claim 3, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a cell-free environment.

30. The method of claim 3, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase *in vitro*.

31. The method of claim 3, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in cell culture.

32. The method of claim 31, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a culture of peripheral blood mononuclear cells.

33. A method for identifying a candidate compound as a suitable pro-drug, comprising:

(a) providing the candidate compound having an esterified phosphonate group;

(b) contacting the candidate compound with GS-7340 Ester Hydrolase to produce a metabolite compound; and

(c) identifying the candidate compound as a suitable pro-drug if the metabolite compound has a phosphonic acid group instead of the esterified phosphonate group of the candidate compound.

34. The method of claim 33, wherein said providing step further comprises monosubstitution of the esterified phosphonate group with an organic acid having an esterified carboxyl group.

35. The method of claim 33, wherein said providing step further comprises monosubstitution of the esterified phosphonate group with an amino acid linked through an amino group to the phosphorus atom, wherein the amino acid has an esterified carboxyl group.

36. The method of claim 33, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound known to have anti-HIV therapeutic activity with an esterified phosphonate or carboxyl group.

37. The method of claim 36, wherein said prototype compound is not a nucleoside, and does not contain a nucleoside base.

38. The method of claim 33, wherein said providing step comprises providing a candidate compound that is an amino acid phosphonoamidate, wherein a carboxyl group of the amino acid is esterified.

39. The method of claim 33, wherein said providing step comprises providing a candidate compound that is substantially stable against extracellular hydrolysis of the esterified group.

40. The method of claim 33, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound.

41. The method of claim 33, further comprising (d) determining the intracellular persistence of the candidate compound.

42. The method of claim 33, further comprising (d) determining the intracellular persistence of the metabolite compound.

43. The method of claim 33, further comprising (d) determining the intracellular persistence of the candidate compound and the metabolite compound.

44. The method of claim 33, further comprising (d) determining the tissue selectivity of the candidate compound.

45. The method of claim 33, further comprising (d) determining the tissue selectivity of the metabolite compound.

46. The method of claim 33, further comprising (d) determining the tissue selectivity of the candidate compound and the metabolite compound.

47. The method of claim 33, further comprising (d) determining the anti-HIV protease activity of the metabolite compound.

48. The method of claim 33, further comprising (d) determining the HIV-inhibition ability of the candidate compound.

49. The method of claim 33, further comprising (d) determining the resistance of HIV to the candidate compound.

50. The method of claim 33, further comprising (d) determining the resistance of HIV to the metabolite compound.

51. The method of claim 33, further comprising (d) determining the resistance of HIV to the candidate compound and the metabolite compound.

52. The method of claim 33, further comprising (d) determining the intracellular residence time of the candidate compound.

53. The method of claim 33, further comprising (d) determining the intracellular residence time of the metabolite compound.

54. The method of claim 33, further comprising (d) determining the intracellular residence time of the candidate compound and the metabolite compound.

55. The method of claim 52, wherein said step of determining the intracellular residence time of the candidate compound comprises determining the half-life of the candidate compound within lymphoid tissue.

56. The method of claim 53, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

57. The method of claim 54, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

58. The method of claim 55, wherein said step of determining the half-life of the candidate compound further comprises determining the half-life of the candidate compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

59. The method of claim 56, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

60. The method of claim 57, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

61. The method of claim 33, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a cell-free environment.

62. The method of claim 33, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase *in vitro*.

63. The method of claim 33, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in cell culture.

64. The method of claim 63, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a culture of peripheral blood mononuclear cells.

65. A method for identifying a candidate compound as a suitable pro-drug, comprising:

(a) providing the candidate compound having an esterified carboxyl group;

(b) contacting the candidate compound with GS-7340 Ester Hydrolase to produce an metabolite compound; and

(c) identifying the candidate compound as a suitable pro-drug if the metabolite compound has a carboxylic acid group instead of the esterified carboxyl group of the candidate compound.

66. The method of claim 65, wherein said providing step comprises providing a candidate compound substituted with an amino acid group, wherein the amino acid has an esterified carboxyl group.

67. The method of claim 65, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound known to have anti-HIV therapeutic activity with an esterified phosphonate or carboxyl group.

68. The method of claim 67, wherein said prototype compound is not a nucleoside, and does not contain a nucleoside base.

69. The method of claim 65, wherein said providing step comprises providing a candidate compound that is an amino acid phosphonoamidate, wherein a carboxyl group of the amino acid is esterified.

70. The method of claim 65, wherein said providing step comprises providing a candidate compound that is substantially stable against extracellular hydrolysis of the esterified group.

71. The method of claim 65, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound.

72. The method of claim 65, further comprising (d) determining the intracellular persistence of the candidate compound.

73. The method of claim 65, further comprising (d) determining the intracellular persistence of the metabolite compound.

74. The method of claim 65, further comprising (d) determining the intracellular persistence of the candidate compound and the metabolite compound.

75. The method of claim 65, further comprising (d) determining the tissue selectivity of the candidate compound.

76. The method of claim 65, further comprising (d) determining the tissue selectivity of the metabolite compound.

77. The method of claim 65, further comprising (d) determining the tissue selectivity of the candidate compound and the metabolite compound.

78. The method of claim 65, further comprising (d) determining the anti-HIV protease activity of the metabolite compound.

79. The method of claim 65, further comprising (d) determining the HIV-inhibition ability of the candidate compound.

80. The method of claim 65, further comprising (d) determining the resistance of HIV to the candidate compound.

81. The method of claim 65, further comprising (d) determining the resistance of HIV to the metabolite compound.

82. The method of claim 65, further comprising (d) determining the resistance of HIV to the candidate compound and the metabolite compound.

83. The method of claim 65, further comprising (d) determining the intracellular residence time of the candidate compound.

84. The method of claim 65, further comprising (d) determining the intracellular residence time of the metabolite compound.

85. The method of claim 65, further comprising (d) determining the intracellular residence time of the candidate compound and the metabolite compound.

86. The method of claim 83, wherein said step of determining the intracellular residence time of the candidate compound comprises determining the half-life of the candidate compound within lymphoid tissue.

87. The method of claim 84, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

88. The method of claim 85, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

89. The method of claim 86, wherein said step of determining the half-life of the candidate compound further comprises determining the half-life of the candidate compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

90. The method of claim 87, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

91. The method of claim 88, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

92. The method of claim 65, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a cell-free environment.

93. The method of claim 65, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase *in vitro*.

94. The method of claim 65, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in cell culture.

95. The method of claim 94, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a culture of peripheral blood mononuclear cells.

96. A method for identifying a candidate compound as a suitable pro-drug, comprising:

(a) providing the candidate compound having an esterified phosphonate group or an esterified carboxyl group;

(b) contacting the candidate compound with an extract of peripheral blood mononuclear cells which has carboxylic ester hydrolase activity but does not cleave alpha-napthyl acetate, to produce a metabolite compound; and

(c) identifying the candidate compound as a suitable pro-drug if the metabolite compound has a phosphonic acid group instead of the esterified phosphonate group of the candidate compound, or a carboxylic acid group instead of the esterified carboxyl group of the candidate compound.

97. The method of claim 96, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound known to have anti-HIV therapeutic activity with an esterified phosphonate or carboxyl group.

98. The method of claim 97, wherein said prototype compound is not a nucleoside, and does not contain a nucleoside base.

99. The method of claim 96, wherein said providing step comprises providing a candidate compound that is an amino acid phosphonoamidate, wherein a carboxyl group of the amino acid is esterified.

100. The method of claim 96, wherein said providing step comprises providing a candidate compound that is substantially stable against extracellular hydrolysis of the esterified group.

101. The method of claim 96, wherein said providing step comprises providing a candidate compound formed by substituting a prototype compound.

102. The method of claim 96, further comprising (d) determining the intracellular persistence of the candidate compound.

103. The method of claim 96, further comprising (d) determining the intracellular persistence of the metabolite compound.

104. The method of claim 96, further comprising (d) determining the intracellular persistence of the candidate compound and the metabolite compound.

105. The method of claim 96, further comprising (d) determining the tissue selectivity of the candidate compound.

106. The method of claim 96, further comprising (d) determining the tissue selectivity of the metabolite compound.

107. The method of claim 96, further comprising (d) determining the tissue selectivity of the candidate compound and the metabolite compound.

108. The method of claim 96, further comprising (d) determining the anti-HIV protease activity of the metabolite compound.

109. The method of claim 96, further comprising (d) determining the HIV-inhibition ability of the candidate compound.

110. The method of claim 96, further comprising (d) determining the resistance of HIV to the candidate compound.

111. The method of claim 96, further comprising (d) determining the resistance of HIV to the metabolite compound.

112. The method of claim 96, further comprising (d) determining the resistance of HIV to the candidate compound and the metabolite compound.

113. The method of claim 96, further comprising (d) determining the intracellular residence time of the candidate compound.

114. The method of claim 96, further comprising (d) determining the intracellular residence time of the metabolite compound.

115. The method of claim 96, further comprising (d) determining the intracellular residence time of the candidate compound and the metabolite compound.

116. The method of claim 113, wherein said step of determining the intracellular residence time of the candidate compound comprises determining the half-life of the candidate compound within lymphoid tissue.

117. The method of claim 114, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

118. The method of claim 115, wherein said step of determining the intracellular residence time of the metabolite compound comprises determining the half-life of the metabolite compound within lymphoid tissue.

119. The method of claim 116, wherein said step of determining the half-life of the candidate compound further comprises determining the half-life of the candidate compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

120. The method of claim 117, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

121. The method of claim 118, wherein said step of determining the half-life of the metabolite compound further comprises determining the half-life of the metabolite compound within helper cells, killer cells, lymph nodes, or peripheral blood mononuclear cells.

122. The method of claim 96, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a cell-free environment.

123. The method of claim 96, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase *in vitro*.

124. The method of claim 96, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in cell culture.

125. The method of claim 124, wherein said contacting step comprises contacting the candidate compound with GS-7340 Ester Hydrolase in a culture of peripheral blood mononuclear cells.

126. A candidate compound identified by the method of claim 1, wherein the candidate compound is an amino acid phosphonoamidate in which a carboxyl group of the amino acid is esterified.

127. A candidate compound identified by the method of claim 33, wherein the candidate compound is an amino acid phosphonoamidate in which a carboxyl group of the amino acid is esterified.

128. A candidate compound identified by the method of claim 65, wherein the candidate compound is an amino acid phosphonoamidate in which a carboxyl group of the amino acid is esterified.

129. A candidate compound identified by the method of claim 96, wherein the candidate compound is an amino acid phosphonoamidate in which a carboxyl group of the amino acid is esterified.

130. A candidate compound identified by the method of claim 1, wherein the candidate compound is substituted with an amino acid group in which a carboxyl group of the amino acid is esterified.

131. A candidate compound identified by the method of claim 33, wherein the candidate compound is substituted with an amino acid group in which a carboxyl group of the amino acid is esterified.

132. A candidate compound identified by the method of claim 65, wherein the candidate compound is substituted with an amino acid group in which a carboxyl group of the amino acid is esterified.

133. A candidate compound identified by the method of claim 96, wherein the candidate compound is substituted with an amino acid group in which a carboxyl group of the amino acid is esterified.

134. The candidate compound of claim 130, wherein the amino group of the amino acid is in the alpha position.

135. The candidate compound of claim 131, wherein the amino group of the amino acid is in the alpha position.

136. The candidate compound of claim 132, wherein the amino group of the amino acid is in the alpha position.

137. The candidate compound of claim 133, wherein the amino group of the amino acid is in the alpha position.

138. A candidate compound identified by the method of claim 1, wherein the esterified phosphonate group is monosubstituted with a hydroxyorganic acid linked to the phosphorus atom through an oxygen atom.

139. The candidate compound of claim 138, wherein the hydroxy group of the hydroxyorganic acid is in the alpha position.

140. A candidate compound identified by the method of claim 1, wherein the candidate compound is substantially stable against extracellular hydrolysis of the esterified group.

141. A candidate compound identified by the method of claim 33, wherein the candidate compound is substantially stable against extracellular hydrolysis of the esterified group.

142. A candidate compound identified by the method of claim 65, wherein the candidate compound is substantially stable against extracellular hydrolysis of the esterified group.

143. A candidate compound identified by the method of claim 96, wherein the candidate compound is substantially stable against extracellular hydrolysis of the esterified group.

144. A method of screening candidate compounds for suitability as anti-HIV therapeutic agents, comprising:

(a) providing a candidate compound identified by the method of claim 1;

(b) determining the anti-HIV activity of the candidate compound; and

(c) determining the intracellular persistence of the candidate compound.

145. A method of screening candidate compounds for suitability as anti-HIV therapeutic agents, comprising:

(a) providing a candidate compound identified by the method of claim 33;

(b) determining the anti-HIV activity of the candidate compound; and

(c) determining the intracellular persistence of the candidate compound.

146. A method of screening candidate compounds for suitability as anti-HIV therapeutic agents, comprising:

(a) providing a candidate compound identified by the method of claim 65;

(b) determining the anti-HIV activity of the candidate compound; and

(c) determining the intracellular persistence of the candidate compound.

147. A method of screening candidate compounds for suitability as anti-HIV therapeutic agents, comprising:

(a) providing a candidate compound identified by the method of claim 96;

(b) determining the anti-HIV activity of the candidate compound; and

(c) determining the intracellular persistence of the candidate compound.

148. The method of claim 144, wherein said step (b) comprises determining the activity of the candidate compound against HIV protease.

149. The method of claim 145, wherein said step (b) comprises determining the activity of the candidate compound against HIV protease.

150. The method of claim 146, wherein said step (b) comprises determining the activity of the candidate compound against HIV protease.

151. The method of claim 147, wherein said step (b) comprises determining the activity of the candidate compound against HIV protease.

152. The method of claim 144, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV.

153. The method of claim 145, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV.

154. The method of claim 146, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV.

155. The method of claim 147, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV.

156. The method of claim 152, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV protease.

157. The method of claim 153, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV protease.

158. The method of claim 154, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV protease.

159. The method of claim 155, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV protease.

160. The method of claim 152, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV integrase.

161. The method of claim 153, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV integrase.

162. The method of claim 154, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV integrase.

163. The method of claim 155, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV integrase.

164. The method of claim 152, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV reverse transcriptase.

165. The method of claim 153, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV reverse transcriptase.

166. The method of claim 154, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV reverse transcriptase.

167. The method of claim 155, wherein said step (b) comprises determining the ability of the candidate compound to inhibit HIV reverse transcriptase.

168. The method of claim 144, wherein said step (b) further comprises determining the resistance of HIV to the candidate compound.

169. The method of claim 144, wherein said step (b) is performed by *in vitro* assay.

170. The method of claim 144, wherein said step (b) further comprises determining the anti-HIV activity of an acid metabolite of the candidate compound.

171. The method of claim 170, wherein said acid metabolite is a carboxylic acid compound formed by esterolytic hydrolysis of the candidate compound.

172. The method of claim 170, wherein said acid metabolite is a phosphonic acid compound formed by esterolytic hydrolysis of the candidate compound.

173. The method of claim 144, wherein said step (c) comprises determining the intracellular residence time of the candidate compound.

174. The method of claim 144, wherein said step (c) further comprises determining the intracellular residence time of an acid metabolite of the candidate compound.

175. The method of claim 144, wherein said acid metabolite is a carboxylic acid compound formed by esterolytic hydrolysis of the candidate compound.

176. The method of claim 144, wherein said acid metabolite is a phosphonic acid compound formed by esterolytic hydrolysis of the candidate compound.

177. The method of claim 144, wherein said step (c) further comprises determining the half-life of the metabolite compound within lymphoid tissue.

178. The method of claim 177, wherein in said step of determining the half-life of the metabolite compound within lymphoid tissue, the lymphoid tissue is selected from the group consisting of helper cells, killer cells, lymph nodes, and peripheral blood mononuclear cells.

179. The method of claim 144, further comprising (d) determining the tissue selectivity of the candidate compound.

180. The method of claim 179, wherein said step (d) further comprises determining the tissue selectivity of an acid metabolite of the candidate compound.